生态毒理学报
Asian Journal of Ecotoxicology
第 15 卷 第 4 期 2020 年 8 月
Vol. 15, No.4 Aug. 2020

DOI: 10.7524/AJE.1673-5897.20190805001
郑晓雨, 袁明俊, 王德高, 等. 基于污水流行病学的毒情研判技术研究进展[J]. 生态毒理学报,2020, 15(4): 79-87
Zheng X Y, Yuan M J, Wang D G, et al. Sewage epidemiology for drug situation assessment [J]. Asian Journal of Ecotoxicology, 2020, 15(4): 79-87 (in Chinese)

基于污水流行病学的毒情研判技术研究进展

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收稿日期:2019-08-05　　**录用日期**:2019-10-16

摘要: 毒情研判是区域性毒情形势的重要衡量方法,一直都是禁毒领域关注的热点和难点。利用污水流行病学建立了以污水样品采集、研究对象稳定性、前处理及分析、校正因子、人口数量和不确定度等为影响因素的数学模型对毒品区域流行趋势、滥用量、合成路线研判及新精神活性物质查缉管控等方面进行毒情研判,具有便捷、客观和实时监测等优势。结合当前研究中滥用量准确度、环境样本种类、范围有限和技术手段等方面存在的问题,指出数学模型的完善以及基于高分辨的非靶向和拟靶向分析技术的优化将成为污水流行病学在毒情研判领域的发展趋势。
关键词: 毒品;新精神活性物质;污水流行病学;毒情研判
文章编号: 1673-5897(2020)4-079-09　　**中图分类号**: X171.5　　**文献标识码**: A

Sewage Epidemiology for Drug Situation Assessment

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Received 5 August 2019　　**accepted** 16 October 2019

Abstract: As an important method for evaluating the drug situation, accurate analysis and assessment have been all along the focus and challenge in the field of drug control. Owing to the particularity of drug crime, it is hard to accurately assess the invisible drug situation. With the advantages of high efficiency, convenience, objectivity and nearly-real time, the forensic epidemiology-based drug situation analysis and assessment models have attracted increasing attention and were extensively applied for estimating the amount of abuse, the population of abuse and drug synthesis as well as the control of new psychoactive substances in recent years. This work reviewed the progress in this research field and the existing problems. The optimization of the mathematical models and analysis techniques are proposed as the focus in the field of forensic epidemiology-based drug situation analysis and assess-

基金项目:国家自然科学基金资助项目(21806022);中央级科研院所基本科研业务费(2018JB042)
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ment in the future.

Keywords: illicit drug; new psychoactive substance; sewage epidemiology; drug situation assessment

毒品滥用问题严重威胁着人体健康、经济发展和社会稳定[1]。毒情研判,是把握禁毒形势发展方向的前提,是贯彻落实中央决策部署和禁毒全局工作的基础,是反映禁毒工作实际情况的关键,一直都是禁毒领域关注的热点和难点。当前我国毒情评估技术主要有统计管理、专家调查、社区调查和毒品检验数据分析等,但数据的收集和分析极为耗时耗财,且对于政策制定存在严重的滞后性,更重要的是毒品犯罪的特殊性使得公安机关很难对隐性毒情进行准确评估。特别是对于国内禁毒工作中的突出问题,如制造合成毒品和新精神活性物质(new psychoactive substances, NPS)的查缉等,还缺乏有效的解决方法。

新精神活性物质又称“策划药”、“实验室毒品”,是指未被国际禁毒公约管制,但其滥用会为公众健康带来威胁的物质,成为继传统毒品和合成毒品之后全球流行的第 3 代毒品。近年来,新精神活性物质的快速发展蔓延已经成为当前全球面临的突出问题,也是毒品犯罪领域打击的重点和难点。新精神活性物质的强成瘾危害性,逃避法律管制等特性为其泛滥推波助澜,多变易变的物质结构和物质属性,使得对其发现和监管仍缺乏及时有效的手段[2]。

基于污水流行病学的毒情分析方法可通过短期或长期采取和检测水、空气和土壤等环境样本,获取吸食毒品类型的变化趋势或新型毒品种类信息,通过测定环境中毒品及其代谢产物的浓度,应用相应数学模型计算,推算出该区域内吸毒人员服用的某种类型的毒品数量,还可以与问卷调查、犯罪统计等传统方法所评估的毒情进行吻合度验证[3-5]。污水流行病学不仅具有准确、便捷、客观和接近实时监测等优势,而且避免了传统调查方法中由于被调查人的误报等情况引起的偏差。同时由于污水流行病学具有高灵敏度等优势,在区域范围内新精神活性物质滥用行为的查缉中发挥重要作用。因此,其在全球范围掀起了研究热潮,在毒情研判评估领域得到了广泛应用[6-8]。

1 污水流行病学的方法学发展(Methodology development of sewage epidemiology)

德国联邦消费者保护和食品安全局于 20 世纪末通过对地表水的分析实现了对常见种类药物滥用情况的宏观研判。污水流行病学的概念由 Daughton[9]于 2001 年首次提出,Zuccato 在 2005 年首次针对可卡因进行实施[10]。随后实战转换为基于市政等污水分析的一种毒情研判技术。

2008 年,欧洲毒品及毒瘾监测中心开始关注并积极推广污水分析法的应用领域。特别是 2012 年以来,基于污水样本的分析技术受到了包括欧洲毒品与毒瘾检测中心(EMCDDA)、联合国毒品与犯罪调查办公室(UNODC)和欧洲污水分析核心成员国(Sewage Analysis CORE Group Europe, SCORE)等国际组织或机构的重视与支持,亚洲[11]、欧洲[12]、非洲[13]、美洲[14-15]和大洋洲[16-17]均有学者在进行该领域的研究,并在诸多方向上取得了长足的发展。

相较于传统流行病学,污水流行病学具有实时监测、采样分析简便、成本低和数据客观等显著优势,同时能够对潜在的新型化合物进行监测。随着研究不断深入,理论方法日趋完善,特别是在污水样品采集、研究对象稳定性、前处理及分析、校正因子、人口数量和不确定度等主要参数方面取得了显著进步(图 1)。

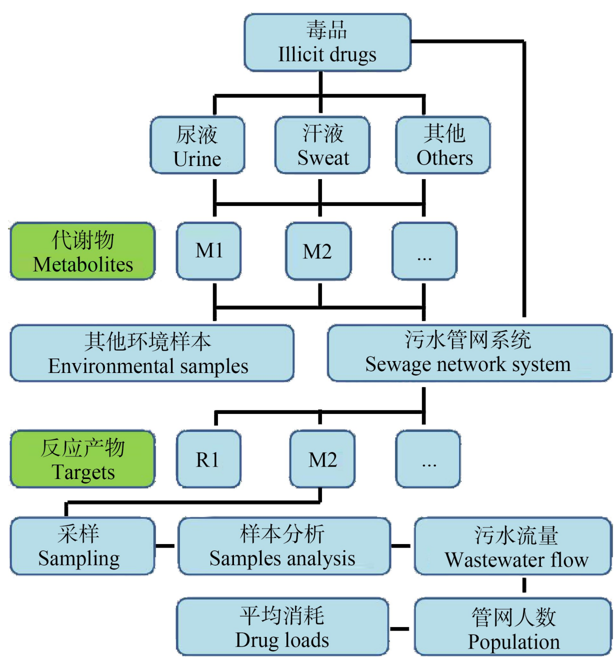

图 1 污水流行病学分析方法

Fig. 1 The workflow of sewage epidemiology

1.1　污水样品采集

污水流行病学主要测定市政污水处理厂的进出水样品中研究对象母体和代谢物的浓度，而污水管道中污水的流量和污水中目标物的浓度并非一成不变，产生的不均匀性可能会导致目标物含量的短期显著变化。研究表明，采样的不确定度主要取决于污染物峰值的数量和采样频率，因此，科学合理的代表性采样是分析结果有意义的先决条件，一般遵循高频率和等流量比例原则。

Ort 等[18]认为浓度变化决定采样频率，流量变化影响采样模式。采样模式分为连续采样和离散采样，其中离散采样主要包括等流量比例、等体积比例和等时间比例采样或即时取样等。定时定量和等流量比例是较为常用的采样模式。其中等流量比例模式可以对单个的子样本进行正确加权，组成复合样本分析得到平均浓度。

实际上，采样频率和采样模式的选择还取决于研究的目的，如分析方法开发、定性检验和定量检验等[19]。当研究目的为分析方法开发或定性检验时，任何一种采样模式都可能是合理的，一般选择在多情况下(夜间/白天、晴天/干燥)进行多次即时取样。而对于定量检验为目的的采样而言，通常是在能反映研究周期内情况的时间跨度内(一般为 24 h 以上)，以等流量比例、等体积比例或等时间比例模式采集后混合样品。依据分析物质和研究内容的不同，取样量也不同，一般 500 mL 即可满足分析需要。

1.2　研究对象稳定性

目标物在下水管网道系统中会经过一系列物理、化学和生物作用，因此，不同生物标志物在不同废水环境中稳定性存在较大差异。研究发现，影响污水存储的主要因素包括温度、pH、微生物量和悬浮颗粒物等[20-22]。一般地，通过添加杀菌剂抑制生物活性，经滤膜过滤后根据目标物的物化性质选择合适的存储条件[19]。对于可卡因[23]、可待因[24]和苯丙胺类[25]毒品均属于高稳定性物质，24 h 内常温(20 ℃)和冷藏(4 ℃)、3 周内冷冻(−25 ℃)存储都可以保持样品的稳定性，样品酸化、添加焦亚硫酸钠或叠氮化钠都有利于样品的存储[19,26]。吗啡本身在冷藏和冷冻条件下稳定性较好，但在常温下会由于海洛因等其他物质的转化造成浓度变化。对于大麻而言，酸性条件下大麻酚酸容易吸附到悬浮颗粒物上，因此一般选择直接冷冻保存[27-28]。总而言之，酸化有利于除四氢大麻酚酸外大部分毒品的稳定性，冷冻保存可以稳定存储 3 周以上。

1.3　前处理及分析

污水中研究对象含量往往较低、干扰成分极多，根据目标物的理化性质选择合适的前处理方法，并采用高灵敏度分析仪器，是实现准确定性定量分析的基本前提。一般地，需加入同位素内标物，经微孔滤膜过滤后使用固相微萃取柱进行净化和浓缩等[25]。当前文献报道中，使用较多的是 Waters 公司的 Oasis 系列产品。根据大多数毒品的极性和解离常数，一般选择 Oasis 系列的混合阳离子交换柱或亲水亲脂平衡交换柱进行前处理，采用液相色谱串联质谱仪进行分析。

1.4　校正因子

校正因子是反演推算中的重要参数，值得说明的是，它并非固定或唯一，需要根据目标物、滥用人群特征和药物代谢等数据进行调整，因此不同研究在进行结果推算中采用不同的校正因子。一般地，校正因子(f_T)计算公式如下：

$$f_T=\sum_{i=1}^{h}\frac{MW_I\times100}{MW_T\times x_h\times R_h}$$

式中：MW_I 和 MW_T 分别为毒品母体和代谢产物(分析对象)的分子量，x_h 是毒品母体通过 h 方式代谢为代谢产物的比例，R_h 是通过 h 途径摄入的比例。

当代谢产物(分析对象)即为毒品母体时，校正因子公式可简化为：

$$f_T=\sum_{i=1}^{h}\frac{100}{x_h\times R_h}$$

1.5　人口数量

人口数量估算是推算人均毒品消耗量和毒品滥用率等毒情研判参数的重要依据，但是由于人口的流动性，对于污水处理厂，特别是旅游型城市污水处理厂对应人口数量的估算一直缺乏公认的权威方法。目前，一般采用设计容量法、污水特征数据和生物标志物等进行估算，但是关于其准确性的进一步研究仍在进行中[29-31]。

1.6　不确定性

尽管污水流行病学能够提供实时、客观和连续的毒品消耗情况，但是这种方法中各种参数的不确定性的来源和控制仍处于研究初期。相较于高斯误差公式，引入的蒙特卡罗等概率分析方法提高了利用污水流行病学的毒情研判技术的可靠性和准确性[29,32]。

2 基于污水流行病学的毒情研判应用(Drug situation assessment with sewage epidemiology)

在基础理论不断完善的同时,基于污水流行病学的毒情研判应用范围也得到了不断发展,包括毒品滥用流行趋势、滥用量评估、合成路线分析和新精神活性物质的查缉等。

2.1 毒品滥用流行趋势的研判

SCORE每年都对欧洲一些大城市进行监测研究,参与的城市从2011年的19个增加到2016年的70余个。研究表明,欧洲西部和南部滥用可卡因较多,而中部和北部则更流行苯丙胺类[33]。数据显示,甲基苯丙胺曾一度在捷克共和国泛滥,而现在则在其他国家流行[3]。

Mastroianni等[34]研究了西班牙巴塞罗那从2011年至2015年的毒品流行趋势,发现大麻和可卡因等更加流行,而海洛因和地西泮消耗量则降低。与欧洲国家相反的是,海洛因在中国普遍滥用,使得污水中吗啡含量远高于可待因。此外,甲基苯丙胺作为中国滥用量最高的毒品[11],近年来在多省市呈逐年递减趋势,同国家禁毒委发布数据一致[35-36]。Zuccato等[37]对意大利8所高中的毒品流行情况进行分析,发现大麻在学生中非常流行,此外少量吸食可卡因和阿片类毒品,未发现苯丙胺、甲基苯丙胺、氯胺酮和甲卡西酮等。奥地利因斯布鲁克医科大学在2016年对因斯布鲁克的毒品滥用情况进行研究,发现可卡因、苯丙胺和二亚甲基双氧安非他明等在周末的滥用量明显高于工作日,阿片类毒品没有显著差异,利多卡因滥用量则在周末出现下降。此外,在音乐节或其他庆祝活动期间,苯丙胺和可卡因消耗量显著增加[38]。

2.2 毒品滥用量的评估

利用对毒品原体或代谢物含量的分析,通过评估反算公式,可以实现对毒品滥用量的评估。欧洲大多数城市均展开了相关研究,主要针对泛滥严重的可卡因[39]、吗啡[13]、苯丙胺[40]和大麻[27]等。从目前报道来看,水体中常见毒品及其代谢物浓度一般为 $ng \cdot L^{-1}$。其中可卡因和吗啡浓度最高可达数百 $ng \cdot L^{-1}$,美沙酮及其代谢物、大麻酚及其衍生物浓度均可达数十 $ng \cdot L^{-1}$。

Bones等[41]利用固相萃取和液相色谱二级质谱联用技术,对都柏林的可卡因滥用进行评估,结果与其他研究保持较好的一致性。Lai等[42]对新西兰奥克兰的2个污水处理厂进行研究,甲基苯丙胺滥用量约为360 mg·(d·1 000 人)$^{-1}$,二亚甲基双氧安非他明为60 mg·(d·1 000 人)$^{-1}$。Wang等[43]发现北京地西泮的消耗量是全国平均水平的3.8倍以上,地表水中地西泮的含量远高于污水处理厂入口浓度,这表明高浓度地西泮废水直接倾倒入地表水中。Postigo等[44]对监狱外污水进行分析,发现美沙酮、阿普唑仑、麻黄碱和大麻二酚的消耗量分别为156、129、46和33剂·(d·1 000 人)$^{-1}$。北京大学李喜青等同广东省中山市局建立了基于污水流行病学的毒情监测实验室,受到国际广泛关注。2019年以来,山东省在全省范围内实施利用污水流行病学进行毒品滥用情况摸底和监测项目,为毒情研判和重点区域监管提供了重要数据支撑。

2.3 毒品合成路线的推断

由于对毒品原料的严格管控,制毒分子往往会改变合成路线、寻求替代化学品。利用污水流行病学对毒品合成路线的推断过程主要是利用质谱对污水中毒品以及合成毒品所需的制毒原料进行分析,或者对污水中毒品及其代谢物的手性进行分析。

荷兰水循环研究所在2016年利用高分辨质谱对污水进行分析,发现以1-苯基-2丙酮为原料通过Leuckart反应可制备苯丙胺,随后首次研判出以苯乙酸为前驱体制造苯丙胺的合成路线。Castrignano等[45]发现与其他欧洲城市中甲基苯丙胺主要为S-(+)型不同的是,奥斯陆污水系统中甲基苯丙胺主要为外消旋体,可以推测其合成路线存在不同之处。此外,通过手性结构分析还可以推测出毒品是直接投入或者是经吸食后排泄进入环境中的[46]。当前这方面研究还较少,但对于从源头打击毒品犯罪具有重要意义。

2.4 新精神活性物质的查缉

大量研究表明,污水流行病学已经成为打击制造和吸食新精神活性物质的有效技术,同时也将为及早发现新精神活性物质,推进相关立法提供信息支撑[47-50]。

Archer等[51]在尿样中检出了二亚甲基双氧安非他明、可卡因、氯胺酮和甲基苯丙胺等7种软毒品以及大麦芽碱、阿拉伯茶碱和甲基异己胺等6种潜在的新精神活性物质,部分新精神活性物质当时在英国尚未被管控。Reid等[52]通过计算机模拟代谢、生物转化和吸附模型等研究,利用高分辨质谱建立了新精神活性物质中生物标记物的分析方法,检测出1-(4-甲氧基苯基)哌嗪盐酸盐等新精神活性物质。

Kinyua 等[53]将污水经固相萃取后利用液相色谱二级质谱检出 2-(3-甲氧基苯基)-2-乙氨基环己酮(MXE)、丁基卡西酮、乙基卡西酮、甲卡西酮、1-(2-噻吩基)-N-甲基-2-丙胺、副甲氧基甲基安非他命和副甲氧基安非他命等 7 种新精神活性物质。Causanilles 等[54]利用液相高分辨质谱在污水中检出了涵盖合成卡西酮类、苯乙胺类和阿片类等在内的 8 种新精神活性物质,其中,1-(3-氯苯基)哌嗪、2,5-二甲氧基-4-溴苯乙胺等尚属首次检出。Bade 等[12,55]利用液相串联时间飞行质谱仪在南澳大利亚州的 2 家污水处理厂检出了 346 种化合物,包括可卡因、甲基苯丙胺和苯丙胺等传统毒品与利多卡因等掺假剂以及亚甲基二氧吡咯戊酮和夫拉卡等多种新精神活性物质。在此基础上,他们分析了澳大利亚的 50 个污水厂,从而对全国新精神活性物质的区域分布情况进行了研判,结果发现,在所有检出的 200 种新精神活性物质中,有 22 种在全国各地均有检出,滥用最严重的为卡西酮类,一半以上地区检出了合成大麻类新精神活性物质。Celma 等[56]首次采用微液相质谱技术对污水中的传统毒品和新精神活性物质进行同时监测,除可卡因、苯丙胺、甲基苯丙胺和氯胺酮外,还检出了丁基酮、甲基甲卡西酮、甲氧麻黄酮和甲基酮等新精神活性物质。该作者指出相对于传统超高效液相质谱技术,微液相质谱技术的检测灵敏度提高了 14 倍,有望在该领域推广应用。

值得注意的是,当前环境研究中对于已知目标物的常规性定性定量分析通常采用靶向分析。利用全二维气相色谱联合飞行时间质谱、傅里叶转换离子回旋共振质谱和液相色谱串联高分辨质谱等高分辨质谱的非靶向分析技术,可不受分析物质信息和标准物质有无的限制[57-60]。对于分析层出不穷的新精神活性物质等潜在的未知精神和麻醉药品,具有显著优势[48,61-63]。在此基础上,基于高分辨质谱的全扫描模式联合液相质谱的多重反应监测模式或气相质谱的选择离子监测模式的拟靶向分析也得到广泛应用[48,64]。Mardal 等[65]利用嫌疑筛查和非靶向筛查建立了新精神活性物质的高分辨质谱数据库,通过不断信息更新可较好地实现新精神活性物质的覆盖,为打击新型毒品犯罪提供了很好的工作思路。

3　存在的问题(Problems)

尽管基于环境样本的分析可以实现对毒品滥用情况较好的研判,但由于污水流行病学发展时间较短,当前还存在一些亟待解决的问题。

3.1　滥用量评估不够准确

基于污水流行病学对毒品滥用量的评估同公开的社会调查一样,存在着一些误差。从图 1 中可以看出其缺陷存在于评估模型建立的各个环节,包括取样、样本保存、检验分析和模型公式等[66-69]。为此,相关工作者就误差产生的主要步骤,包括毒品进入环境样本的方式[3]、毒品的排泄率[70-71]、手性分子比例[72]、毒品及代谢物与环境之间的作用关系[19-20]以及生物标记物的选择[73]等方面展开了大量研究。

3.2　环境样本种类有限

目前利用流行病学对毒品滥用的研判重点研究了水体,往往忽视了基于固体和气体环境样本分析的毒情研判[74-75]。Subedi 和 Kannan[76]利用电喷雾质谱对美国奥尔巴尼地区污水处理厂的污水和污泥中的可卡因和苯丙胺进行研究。研究表明,人均可卡因使用量达到之前的美国污水研究结论的 4 倍,而苯丙胺的滥用量约为之前研究结论的 6 倍。事实上,Cecinato 和 Balducci[77]在 2007 年就首次对罗马和塔兰托空气中的可卡因进行研究,并发现其浓度与当地的可卡因消耗量有直接关系,随后在圣地亚哥等地空气中均检出了可卡因成分[78]。

3.3　适用范围有限

通过环境样本分析对毒情进行的研判主要研究了某区域内毒品吸食滥用情况,而对于危害性更大、隐蔽性更强的制毒犯罪往往缺乏有效的打击手段。当前有报道称,由于制毒工厂周围环境中土壤、空气和水受到污染,严重影响到附近居民生活,而被公安机关查获,但并未有系统的技术手段通过环境样本分析对制毒案件形成打击态势。此外,由于污水流行病学是利用污水中目标物的检验对毒品进行反演推算,而新精神活性物质层出不穷,使得研究工作者对新精神活性物质的研究还不够深入,缺乏母体和污水中目标物成分的关联性研究。利用污水流行病学对新精神活性物质进行查缉需要研究毒品母体在不同吸食途径下的药代动力学和代谢产物,以及母体和代谢产物与环境介质的交互作用关系等。

3.4　检验技术手段仍待发展

随着科技的发展,新技术、新仪器和新方法不断出现。基于色谱、质谱的靶向和非靶向分析已经广泛应用于未知目标物的检验鉴定中,但存在需要已知目标物信息、标准物质以及灵敏度低、重现性低等缺陷。在此基础上发展起来的拟靶向和嫌疑筛查技术结合了靶向和非靶向技术的优点,但也存在不完

全适合于未知物的高通量定性定量分析等问题。

4 展望(Prospect)

污水流行病学方兴未艾,其对毒品流行趋势及相对滥用量近乎实时的监测是其他方法所无法比拟的。因此,基于污水流行病学的毒情研判技术必将成为禁毒工作中广泛应用的关键技术。

鉴于当前研究进展,笔者认为污水流行病学领域的研究将集中在以下几方面。

(1)分析并校正评估模型中的误差和不确定度。这主要包括毒品的代谢组学研究、手性分析方法研究、毒品及代谢物与环境之间的相互作用等。

(2)新精神活性物质和未知代谢物的检验分析方法研究。笔者相信,基于高分辨质谱的非靶向、拟靶向和嫌疑筛查分析技术将成为利用污水流行病学对新精神活性物质和未知代谢物进行查缉、检验领域的研究热点。

此外,通过进一步的完善和深入的研究,处于发展期的污水流行病学将在更为广泛的领域发挥作用。

(1)经污水处理厂处理后的水体中仍存在一定量的毒品及其代谢物,事实上,毒品及其代谢物普遍存在于地表水和饮用水中,其对生态系统和人类健康影响尚不得而知,亟需开展系统性研究。

(2)通过进一步丰富环境样本的种类,包括水、土壤和大气等,并深入挖掘其中痕量涉毒物质成分与制毒案件的作用机制与关系规律,从而形成对危害性大、隐蔽性强的制毒案件具有有效打击威慑的技术手段将成为必然趋势。

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